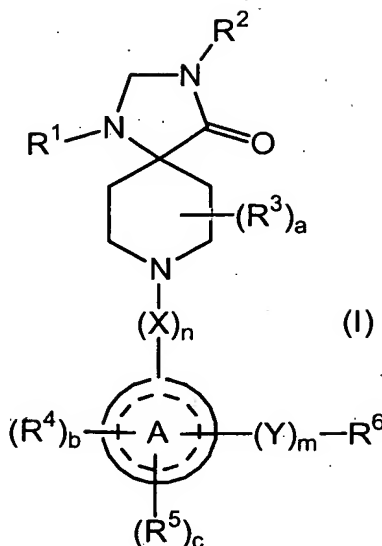


What is claimed is:

1. A compound of the formula



wherein

- 5 R^1 is selected from the group consisting of hydrogen, C_{1-6} alkyl, aryl and aralkyl;

wherein the aryl or aralkyl group is optionally substituted with one to four substituents independently selected from halogen, C_{1-6} alkyl, halogenated C_{1-6} alkyl, C_{1-6} alkoxy, nitro, amino, $(C_{1-6}$ alkyl)amino, $di(C_{1-6}$ alkyl)amino, C_{1-6} alkylsulfonyl, amido, $(C_{1-6}$ alkyl)amido, $di(C_{1-6}$ alkyl)amido, sulfonyl,

- 10 aminosulfonyl, $(C_{1-6}$ alkyl)aminosulfonyl, $di(C_{1-6}$ alkyl)aminosulfonyl or C_{3-8} cycloalkyl;

R^2 is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyamino C_{1-6} alkyl, aminocarbonyl C_{1-6} alkyl, C_{1-6} alkoxycarbonyl C_{1-6} alkyl, aryl, C_{3-8} cycloalkyl, partially unsaturated carbocyclyl, heteroaryl, heterocycloalkyl, C_{1-6} aralkyl, carbocyclyl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocycloalkyl C_{1-6} alkyl and phthalimidoyl C_{1-6} alkyl;

- 15 C_{1-6} alkylamino, $di(C_{1-6}$ alkyl)amino, hydroxy C_{1-6} alkylamino, amino C_{1-6} alkylamino, C_{1-6} alkylamino C_{1-6} alkylamino or $di(C_{1-6}$ alkyl)amino C_{1-6} alkylamino,

wherein the alkyl group is optionally substituted with one to two substituents independently selected from hydroxy, carboxy, cyano, amino, C_{1-6} alkylamino, $di(C_{1-6}$ alkyl)amino, hydroxy C_{1-6} alkylamino, amino C_{1-6} alkylamino, C_{1-6} alkylamino C_{1-6} alkylamino or $di(C_{1-6}$ alkyl)amino C_{1-6} alkylamino,

wherein the aryl, cycloalkyl, carbocyclyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to four substituents independently

selected from halogen, C₁₋₆alkyl, halogenated C₁₋₆alkyl, C₁₋₆alkoxy, nitro, amino, (C₁₋₆alkyl)amino, di(C₁₋₆alkyl)amino, C₁₋₆alkylsulfonyl, amido, (C₁₋₆alkyl)amido, di(C₁₋₆alkyl)amido, sulfonyl, aminosulfonyl, (C₁₋₆alkyl)aminosulfonyl, di(C₁₋₆alkyl)aminosulfonyl or C₁₋₄alkoxycarbonyl;

5 a is an integer from 0 to 2;

R³ is selected from the group consisting of C₁₋₄alkyl and hydroxy C₁₋₄alkyl;

n is an integer from 0 to 1;

X is selected from the group consisting of C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₄alkyl-

10 O and C₂₋₄alkyl-S;

wherein the alkyl group is optionally substituted with one to two substituents independently selected from fluoro, C₁₋₆alkyl, fluorinated C₁₋₆alkyl, C₁₋₆alkoxy, nitro, amino, (C₁₋₆alkyl)amino, di(C₁₋₆alkyl)amino, C₁₋₆alkylsulfonyl, amido, (C₁₋₆alkyl)amido, di(C₁₋₆alkyl)amido, sulfonyl, aminosulfonyl, (C₁₋₆alkyl)aminosulfonyl or di(C₁₋₆alkyl)aminosulfonyl;

15 and wherein X is C₂₋₄alkyl-O or C₂₋₄alkyl-S, the X group is incorporated into the molecule such that the C₂₋₄alkyl is bound directly to the piperidine portion of the molecule;



A is selected from the group consisting of phenyl, a five membered heteroaryl and a six membered heteroaryl;

20 b is an integer from 0 to 1;

R⁴ is selected from the group consisting of aryl, C₃₋₈cycloalkyl, partially unsaturated carbocyclyl, heteroaryl and heterocycloalkyl;

c is an integer from 0 to 3;

25 R⁵ is selected from the group consisting of halogen, C₁₋₆alkyl, halogenated C₁₋₆alkyl, C₁₋₆alkoxy, nitro, amino, (C₁₋₆alkyl)amino, di(C₁₋₆alkyl)amino, C₁₋₆alkylsulfonyl, amido, (C₁₋₆alkyl)amido, di(C₁₋₆alkyl)amido, sulfonyl, aminosulfonyl, (C₁₋₆alkyl)aminosulfonyl or di(C₁₋₆alkyl)aminosulfonyl;

m is an integer from 0 to 1;

30 Y is selected from the group consisting of C₁₋₄alkyl, C₂₋₄alkenyl, O, S, NH, N(C₁₋₄alkyl), C₁₋₆alkyl-O, C₁₋₆alkyl-S, O-C₁₋₆alkyl and S-C₁₋₆alkyl-S;

R^6 is selected from the group consisting of aryl, partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl, heterocycloalkyl and benzoyloxyphenyl;

wherein the aryl, partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to four substituents independently selected from halogen, hydroxy, C_{1-6} alkyl, halogenated C_{1-6} alkyl, C_{1-6} alkoxy, nitro, amino, $(C_{1-6}$ alkyl)amino, di(C_{1-6} alkyl)amino, C_{1-6} alkylsulfonyl, amido, $(C_{1-6}$ alkyl)amido, di(C_{1-6} alkyl)amido, sulfonyl, aminosulfonyl, $(C_{1-6}$ alkyl)aminosulfonyl, di(C_{1-6} alkyl)aminosulfonyl or triphenylmethyl;

provided that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X is CH_2 ,



is phenyl, b is 0, c is 0 and m is 0, then R^6 is selected from the group consisting of partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl, heterocycloalkyl, benzoyloxyphenyl and substituted aryl;

wherein the aryl, partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to four substituents independently selected from halogen, C_{1-6} alkyl, halogenated C_{1-6} alkyl, C_{1-6} alkoxy, nitro, amino, $(C_{1-6}$ alkyl)amino, di(C_{1-6} alkyl)amino, C_{1-6} alkylsulfonyl, amido, $(C_{1-6}$ alkyl)amido, di(C_{1-6} alkyl)amido, sulfonyl, aminosulfonyl, $(C_{1-6}$ alkyl)aminosulfonyl, di(C_{1-6} alkyl)aminosulfonyl or

triphenylmethyl;

provided further that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X



is C_{1-3} alkyl, is phenyl, b is 0, c is 0 and m is 0, then R^6 is not substituted thiazolyl; wherein the substituent on the thiazolyl is selected from amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino or nitro;

provided further that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X



is CH_2 , b is 0, c is 0 and m is 0, and R^6 is phenyl, then is not imidazolyl or pyrrolyl;

and pharmaceutically acceptable salts thereof.

2. A compound as in Claim 1 wherein

R^1 is selected from the group consisting of C_{1-4} alkyl, aryl and aralkyl;

wherein the aryl or aralkyl group is optionally substituted with one to

5 three substituents independently selected from halogen, C_{1-4} alkyl, fluorinated C_{1-4} alkyl, C_{1-4} alkoxy, amino, $(C_{1-4}$ alkyl)amino, $di(C_{1-4}$ alkyl)amino, amido, $(C_{1-4}$ alkyl)amido, $di(C_{1-4}$ alkyl)amido or C_{5-7} cycloalkyl;

R^2 is selected from the group consisting of hydrogen, C_{1-4} alkyl,

10 hydroxyamino C_{1-4} alkyl, aminocarbonyl C_{1-4} alkyl, C_{1-4} alkoxycarbonyl C_{1-4} alkyl, aryl, C_{5-7} cycloalkyl, heteroaryl, heterocycloalkyl, C_{1-4} aralkyl, heteroaryl C_{1-4} alkyl, heterocycloalkyl C_{1-4} alkyl and phthalimidoyl C_{1-4} alkyl;

wherein the alkyl group is optionally substituted with one to two

substituents independently selected from hydroxy, carboxy, cyano, amino, C_{1-4} alkylamino, $di(C_{1-4}$ alkyl)amino, hydroxy C_{1-4} alkylamino, amino C_{1-4} alkylamino, 15 C_{1-4} alkylamino C_{1-4} alkylamino or $di(C_{1-4}$ alkyl)amino C_{1-6} alkylamino,

wherein the aryl, cycloalkyl, heteroaryl or heterocycloalkyl group is

optionally substituted with one to two substituents independently selected from halogen, C_{1-4} alkyl, fluorinated C_{1-4} alkyl, C_{1-4} alkoxy, amino, $(C_{1-4}$ alkyl)amino, $di(C_{1-4}$ alkyl)amino, amido, $(C_{1-4}$ alkyl)amido, $di(C_{1-4}$ alkyl)amido or C_{1-}

20 4 alkoxycarbonyl;

a is an integer from 0 to 1;

R^3 is selected from the group consisting of C_{1-4} alkyl and hydroxy C_{1-}

4 alkyl;

n is an integer from 0 to 1;

25 X is selected from the group consisting of C_{1-6} alkyl, C_{2-4} alkyl-O and C_{2-4} alkyl-S;

wherein the alkyl group is optionally substituted with one to two

substituents independently selected from fluoro, C_{1-4} alkyl, fluorinated C_{1-4} alkyl, C_{1-4} alkoxy, amino, $(C_{1-4}$ alkyl)amino or $di(C_{1-4}$ alkyl)amino;

30 and wherein X is C_{2-4} alkyl-O or C_{2-4} alkyl-S, the X group is incorporated into the molecule such that the C_{2-4} alkyl is bound directly to the piperidine portion of the molecule;



is selected from the group consisting of phenyl, a five membered heteroaryl and a six membered heteroaryl;

b is an integer from 0 to 1;

R^4 is selected from the group consisting of aryl, C_{5-7} cycloalkyl, heteroaryl
5 and heterocycloalkyl;

c is an integer from 0 to 2;

R^5 is selected from the group consisting of halogen, C_{1-4} alkyl, fluorinated C_{1-4} alkyl, C_{1-4} alkoxy, nitro, amino, $(C_{1-4}$ alkyl)amino, di(C_{1-4} alkyl)amino, C_{1-4} alkylsulfonyl, amido, $(C_{1-4}$ alkyl)amido, di(C_{1-4} alkyl)amido,
10 sulfonyl, aminosulfonyl, $(C_{1-4}$ alkyl)aminosulfonyl or di(C_{1-4} alkyl)aminosulfonyl;
m is an integer from 0 to 1;

Y is selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, O, S, NH, $N(C_{1-4}$ alkyl), C_{1-6} alkyl-O, C_{1-6} alkyl-S, O- C_{1-6} alkyl and S- C_{1-6} alkyl-S;

R^6 is selected from the group consisting of aryl, partially unsaturated
15 carbocyclyl, C_{3-8} cycloalkyl, heteroaryl, heterocycloalkyl and benzoyloxyphenyl;
wherein the aryl, partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to two substituents independently selected from halogen, hydroxy, C_{1-4} alkyl, fluorinated C_{1-4} alkyl, C_{1-4} alkoxy, nitro, amino, $(C_{1-4}$ alkyl)amino, di(C_{1-4} alkyl)amino, C_{1-4} alkylsulfonyl, amido, $(C_{1-4}$ alkyl)amido, di(C_{1-4} alkyl)amido,
20 sulfonyl, aminosulfonyl, $(C_{1-4}$ alkyl)aminosulfonyl, di(C_{1-4} alkyl)aminosulfonyl or triphenylmethyl;

provided that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X is CH_2 ,




is phenyl, b is 0, c is 0 and m is 0, then R^6 is selected from the group
25 consisting of partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl, heterocycloalkyl, benzoyloxyphenyl and substituted aryl;


wherein the aryl, partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to four substituents independently selected from halogen, C_{1-6} alkyl, halogenated C_{1-6} alkyl, C_{1-6} alkoxy, nitro, amino, $(C_{1-6}$ alkyl)amino, di(C_{1-6} alkyl)amino, C_{1-6} alkyl,
30

₆alkylsulfonyl, amido, (C₁₋₆alkyl)amido, di(C₁₋₆alkyl)amido, sulfonyl, aminosulfonyl, (C₁₋₆alkyl)aminosulfonyl, di(C₁₋₆alkyl)aminosulfonyl or triphenylmethyl;

provided further that when a is 0, R¹ is phenyl, R² is hydrogen, n is 1, X

5 is C₁₋₃alkyl,  is phenyl, b is 0, c is 0 and m is 0, then R⁶ is not substituted thiazolyl; wherein the substituent on the thiazolyl is selected from amino, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino or nitro;

provided further that when a is 0, R¹ is phenyl, R² is hydrogen, n is 1, X

10 is CH₂, b is 0, c is 0 and m is 0, and R⁶ is phenyl, then  is not imidazolyl or pyrrolyl; and pharmaceutically acceptable salts thereof.

3. A compound as in Claim 2 wherein

R¹ is selected from the group consisting of C₁₋₄alkyl, aryl and aralkyl;

15 wherein the aryl group is optionally substituted with one to three substituent independently selected from halogen, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl and C₅₋₆cycloalkyl;

20 R² is selected from the group consisting of hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, cyanoC₁₋₄alkyl, aminoC₁₋₄alkyl, C₁₋₄alkylaminoC₁₋₄alkyl, di(C₁₋₄alkyl)aminoC₁₋₄alkyl, aminocarbonylC₁₋₄alkyl, carboxyC₁₋₄alkyl, C₁₋₄alkoxycarbonylC₁₋₄alkyl, phthalimidylethyl and C₁₋₄alkoxycarbonyl-oxazolylC₁₋₄alkyl;

a is an integer from 0 to 1;

R³ is selected from the group consisting of C₁₋₄alkyl;

25 n is 1;

X is selected from the group consisting of C₁₋₄alkyl and C₂₋₄alkyl-O;

wherein X is C₂₋₄alkyl-O, the X group is incorporated into the molecule such that the C₂₋₄alkyl portion is bound directly to the piperidine portion of the molecule;



is selected from the group consisting of phenyl and heteroaryl;

b is 0;

c is an integer from 0 to 2;

R^5 is selected from the group consisting of halogen, fluorinated C_{1-4} alkyl

5 and C_{1-4} alkyl;

m is an integer from 0 to 1;

Y is selected from the group consisting of O, C_{1-4} alkyl-O, C_{2-4} alkenyl and C_{1-4} alkyl;

10 R^6 is selected from the group consisting of aryl, partially unsaturated carbocyclyl, heteroaryl, heterocycloalkyl and benzoyloxyphenyl;

wherein the aryl, heteroaryl or heterocycloalkyl is optionally substituted with one to two substituents independently selected from halogen, acetyl, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, cyano, nitro, oxo, t-butoxycarbonyl or triphenylmethyl;

15 provided that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X is CH_2 ,



is phenyl, b is 0, c is 0 and m is 0, then R^6 is selected from the group consisting of partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl, heterocycloalkyl, benzoyloxyphenyl and substituted aryl;


20 wherein the aryl, heteroaryl or heterocycloalkyl is optionally substituted with one to two substituents independently selected from halogen, acetyl, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, cyano, nitro, oxo, t-butoxycarbonyl or triphenylmethyl;

provided further that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X



25 is C_{1-3} alkyl, is phenyl, b is 0, c is 0 and m is 0, then R^6 is not substituted thiazolyl; wherein the substituent on the thiazolyl is selected from amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino or nitro;

provided further that when a is 0, R¹ is phenyl, R² is hydrogen, n is 1, X

is CH₂, b is 0, c is 0 and m is 0, and R⁶ is phenyl, then  is not imidazolyl or pyrrolyl;

and pharmaceutically acceptable salts thereof.

5

4. A compound as in Claim 3 wherein

R¹ is selected from the group consisting of n-propyl, phenyl, 4-fluorophenyl, 3-bromophenyl, 3-chlorophenyl, 3-trifluoromethylphenyl, 4-methylphenyl, 4-methoxyphenyl, 4-cyclopentylphenyl, 4-chloro-3-methylphenyl, 4-fluoro-3,5-dimethylphenyl and benzyl;

10

R² is selected from the group consisting of hydrogen, methyl, cyanomethyl, 2-hydroxyethyl, aminoethyl, dimethylaminoethyl, diethylaminoethyl, aminocarbonylmethyl, carboxymethyl, methoxycarbonylmethyl, phthalimidylethyl and 4-methoxycarbonyl-5-

15

oxazolylmethyl;

a is an integer from 0 to 1;


R³ is methyl;

n is 1;

X is selected from the group consisting of CH₂, and CH₂CH₂,

20 CH₂CH₂CH₂, CH₂CH₂CH₂CH₂ and CH₂CH₂-O;



 is selected from the group consisting of phenyl, furyl, thienyl, pyridyl and pyrazolyl;

b is 0;

c is an integer from 0 to 2;

25

R⁵ is selected from the group consisting of fluoro, chloro, trifluoromethyl and methyl;

m is an integer from 0 to 1;

Y is selected from the group consisting of O, CH₂-O, CH=CH and CH₂;

30 R⁶ is selected from the group consisting of 3-methylphenyl, 4-methylphenyl, 3,5-dichlorophenyl, 4-methoxyphenyl, 3-trifluoromethylphenyl, 3-

pyridyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyrrolyl, 1-naphthyl, 2-naphthyl, 2-(1-Boc-pyrrolyl), 1-(1,2,3,4-tetrahydronaphthyl), phenyl, 4-dimethylaminophenyl, 4-pyridyl, 3-quinolinyl, 2-benzothienyl, 2-benzofuryl, 5-indolyl, 2-thiazolyl, 5-chloro-2-thienyl, 5-acetyl-2-thienyl, 5-methyl-2-thienyl, 5-cyano-2-thienyl, 4-methyl-2-thienyl, 3,5-dimethyl-4-isoxazolyl, 3-pyridyl, 4-chlorophenyl, 1-(5,6,7,8-tetrahydronaphthyl), 4-hydroxy, 1-piperidinyl, 1-(1,2,3,4-tetrahydroquinolinyl), 2-(1,2,3,4-tetrahydroisoquinolinyl), 1-pyrrolidinyl, 1-phthalimidoyl, 1-imidazolyl, 3-imidazolyl, 1-triphenylmethyl-3-imidazolyl, 1-(2-piperidinoyl), 3-chlorophenyl, 4-nitrophenyl, 4-bromophenyl, 4-chlorophenyl and benzoyloxyphenyl;

provided that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X is CH_2 ,



is phenyl, b is 0, c is 0 and m is 0, then R^6 is not phenyl; and pharmaceutically acceptable salts thereof.

5. A compound as in Claim 4 wherein

R^1 is selected from the group consisting of phenyl, 4-fluorophenyl, 3-trifluoromethylphenyl, 4-methylphenyl, 3-bromophenyl, 3-chlorophenyl, 4-chloro-3-methylphenyl and 4-fluoro-3,5-dimethylphenyl;

R^2 is selected from the group consisting of hydrogen, methyl, cyanomethyl, 2-hydroxyethyl, aminoethyl, dimethylaminoethyl, diethylaminoethyl, aminocarbonylmethyl, carboxymethyl, methoxycarbonylmethyl and 4-methoxycarbonyl-5-oxazolylmethyl;

X is selected from the group consisting of CH_2 , and CH_2CH_2 , $CH_2CH_2CH_2$ and $CH_2CH_2CH_2CH_2$;

c is an integer from 0 to 1;

R^5 is selected from the group consisting of fluoro, trimethylphenyl and methyl;



is selected from the group consisting of phenyl, furyl, thienyl and pyrazolyl;

Y is selected from the group consisting of O, CH_2-O and $CH=CH$;

R^6 is selected from the group consisting of 4-methylphenyl, 3,5-dichlorophenyl, 4-methoxyphenyl, 3-trifluoromethylphenyl, 3-pyridyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyrrolyl, 1-naphthyl, 2-naphthyl, 1-(1,2,3,4-tetrahydronaphthyl), phenyl, 2-thiazolyl, 5-chloro-2-thienyl, 5-methyl-2-thienyl, 4-methyl-2-thienyl, 3,5-dimethyl-4-isoxazolyl, 4-chlorophenyl, 4-bromophenyl and 4-chlorophenyl;

provided that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X is CH_2 ,



is phenyl, b is 0, c is 0 and m is 0, then R^6 is not phenyl; and pharmaceutically acceptable salts thereof.

10

6. A compound as in Claim 5 wherein

R^1 is selected from the group consisting of phenyl, 4-fluorophenyl, 3-trifluoromethylphenyl, 4-methylphenyl, 3-bromophenyl and 4-chloro-3-methylphenyl;

15

X is selected from the group consisting of CH_2 , and CH_2CH_2 and $CH_2CH_2CH_2$;



is selected from the group consisting of phenyl and thienyl;

R^5 is fluoro;

m is an integer from 0 to 1;

20

Y is O;

R^6 is selected from the group consisting of phenyl, 3-pyridyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyrrolyl, 2-thiazolyl and 4-methyl-2-thienyl;

provided that when a is 0, R^1 is phenyl, R^2 is hydrogen, n is 1, X is CH_2 ,



is phenyl, b is 0, c is 0 and m is 0, then R^6 is not phenyl; and pharmaceutically acceptable salts thereof.

25

7. A compound as in Claim 6 wherein

R^1 is selected from the group consisting of phenyl and 4-fluorophenyl;

R^2 is selected from the group consisting of hydrogen, methyl, cyanomethyl, 2-hydroxyethyl, dimethylaminoethyl, aminocarbonylmethyl and methoxycarbonylmethyl;



is phenyl;

5 R^6 is selected from the group consisting of 2-furyl, 2-thienyl and 3-thienyl;

and pharmaceutically acceptable salts thereof.

8. A compound as in Claim 1 wherein

10 R^1 is selected from the group consisting of hydrogen, C_{1-6} alkyl and aryl; wherein the aryl group is optionally substituted with one to four substituents independently selected from halogen, C_{1-6} alkyl, halogenated C_{1-6} alkyl, C_{1-6} alkoxy, nitro, amino, $(C_{1-6}alkyl)amino$, $di(C_{1-6}alkyl)amino$, $C_{1-6}alkylsulfonyl$, amido, $(C_{1-6}alkyl)amido$, $di(C_{1-6}alkyl)amido$, sulfonyl, 15 aminosulfonyl, $(C_{1-6}alkyl)aminosulfonyl$, $di(C_{1-6}alkyl)aminosulfonyl$ or $C_{3-8}cycloalkyl$;

R^2 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, hydroxyamino $C_{1-6}alkyl$, aminocarbonyl $C_{1-6}alkyl$, $C_{1-6}alkoxycarbonylC_{1-6}alkyl$, aryl, $C_{3-8}cycloalkyl$, partially unsaturated carbocyclyl, 20 heteroaryl, heterocycloalkyl, $C_{1-6}aralkyl$, carbocyclyl $C_{1-6}alkyl$, heteroaryl $C_{1-6}alkyl$, heterocycloalkyl $C_{1-6}alkyl$ and phthalimidoyl $C_{1-6}alkyl$;

wherein the alkyl group is optionally substituted with one to two substituents independently selected from hydroxy, carboxy, cyano, amino, $C_{1-6}alkylamino$, $di(C_{1-6}alkyl)amino$, hydroxy $C_{1-6}alkylamino$, amino $C_{1-6}alkylamino$, 25 $C_{1-6}alkylaminoC_{1-6}alkylamino$ or $di(C_{1-6}alkyl)aminoC_{1-6}alkylamino$,

wherein the aryl, cycloalkyl, carbocyclyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to four substituents independently selected from halogen, $C_{1-6}alkyl$, halogenated $C_{1-6}alkyl$, $C_{1-6}alkoxy$, nitro, amino, $(C_{1-6}alkyl)amino$, $di(C_{1-6}alkyl)amino$, $C_{1-6}alkylsulfonyl$, amido, $(C_{1-6}alkyl)amido$, $di(C_{1-6}alkyl)amido$, sulfonyl, aminosulfonyl, $(C_{1-6}alkyl)aminosulfonyl$ or $di(C_{1-6}alkyl)aminosulfonyl$;

30

a is an integer from 0 to 2;

R^3 is selected from the group consisting of C_{1-4} alkyl and hydroxy C_{1-4} alkyl;


n is an integer from 0 to 1;

5 X is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-4} alkyl-O and C_{2-4} alkyl-S;

wherein the alkyl group is optionally substituted with one to two substituents independently selected from fluoro, C_{1-6} alkyl, fluorinated C_{1-6} alkyl, C_{1-6} alkoxy, nitro, amino, $(C_{1-6}$ alkyl)amino, di $(C_{1-6}$ alkyl)amino, C_{1-6} alkylsulfonyl, 10 amido, $(C_{1-6}$ alkyl)amido, di $(C_{1-6}$ alkyl)amido, sulfonyl, aminosulfonyl, $(C_{1-6}$ alkyl)aminosulfonyl or di $(C_{1-6}$ alkyl)aminosulfonyl;

and wherein X is C_{2-4} alkyl-O or C_{2-4} alkyl-S, the X group is incorporated into the molecule such that the C_{2-4} alkyl is bound directly to the piperidine portion of the molecule;



15  is selected from the group consisting of phenyl, a five membered heteroaryl and a six membered heteroaryl;

b is an integer from 0 to 1;

R^4 is selected from the group consisting of aryl, C_{3-8} cycloalkyl, partially unsaturated carbocyclyl, heteroaryl and heterocycloalkyl;

20 c is an integer from 0 to 3;

R^5 is selected from the group consisting of halogen, C_{1-6} alkyl, halogenated C_{1-6} alkyl, C_{1-6} alkoxy, nitro, amino, $(C_{1-6}$ alkyl)amino, di $(C_{1-6}$ alkyl)amino, C_{1-6} alkylsulfonyl, amido, $(C_{1-6}$ alkyl)amido, di $(C_{1-6}$ alkyl)amido, sulfonyl, aminosulfonyl, $(C_{1-6}$ alkyl)aminosulfonyl or di $(C_{1-6}$ alkyl)aminosulfonyl;

25 m is an integer from 0 to 1;

Y is selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, O, S, NH, N $(C_{1-4}$ alkyl), C_{1-6} alkyl-O, C_{1-6} alkyl-S, O- C_{1-6} alkyl and S- C_{1-6} alkyl-S;

R^6 is selected from the group consisting of aryl, partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl, heterocycloalkyl and benzoyloxyphenyl;

30 wherein the aryl, partially unsaturated carbocyclyl, C_{3-8} cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to four

substituents independently selected from halogen, hydroxy, C₁₋₆alkyl, halogenated C₁₋₆alkyl, C₁₋₆alkoxy, nitro, amino, (C₁₋₆alkyl)amino, di(C₁₋₆alkyl)amino, C₁₋₆alkylsulfonyl, amido, (C₁₋₆alkyl)amido, di(C₁₋₆alkyl)amido, sulfonyl, aminosulfonyl, (C₁₋₆alkyl)aminosulfonyl or di(C₁₋₆alkyl)aminosulfonyl;

5 provided that when a is 0, R¹ is phenyl, R² is hydrogen, n is 1, X is CH₂,



is phenyl, b is 0, c is 0 and m is 0, then R⁶ is selected from the group consisting of partially unsaturated carbocyclyl, C₃₋₈cycloalkyl, heteroaryl, heterocycloalkyl and substituted aryl;

10 wherein the aryl, partially unsaturated carbocyclyl, C₃₋₈cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one to four substituents independently selected from halogen, C₁₋₆alkyl, halogenated C₁₋₆alkyl, C₁₋₆alkoxy, nitro, amino, (C₁₋₆alkyl)amino, di(C₁₋₆alkyl)amino, C₁₋₆alkylsulfonyl, amido, (C₁₋₆alkyl)amido, di(C₁₋₆alkyl)amido, sulfonyl, aminosulfonyl, (C₁₋₆alkyl)aminosulfonyl or di(C₁₋₆alkyl)aminosulfonyl;

15 provided further that when a is 0, R¹ is phenyl, R² is hydrogen, n is 1, X



is C₁₋₃alkyl, is phenyl, b is 0, c is 0 and m is 0, then R⁶ is not substituted thiazolyl; wherein the substituent on the thiazolyl is selected from amino, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino or nitro;

provided further that when a is 0, R¹ is phenyl, R² is hydrogen, n is 1, X



20 is CH₂, b is 0, c is 0 and m is 0, and R⁶ is phenyl, then is not imidazolyl or pyrrolyl;

and pharmaceutically acceptable salts thereof.

9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of Claim 1.

10. A pharmaceutical composition made by mixing a compound of Claim 1 and a pharmaceutically acceptable carrier.

11. A process for making a pharmaceutical composition comprising mixing a compound of Claim 1 and a pharmaceutically acceptable carrier.
- 5 12. A method of treating a disorder mediated by the ORL-1 receptor, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.
- 10 13. The method of Claim 12, wherein the disorder mediated by the ORL-1 receptor is selected from the group consisting of anxiety, depression, substance abuse, neuropathic pain, acute pain, migraine, asthma, cough and improved cognition.
- 15 14. A method of treating a disorder mediated by the ORL-1 receptor, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the composition of Claim 9.
- 20 15. A method of treating a condition selected from the group consisting of anxiety, depression, substance abuse, neuropathic pain, acute pain, migraine, asthma, cough and improved cognition, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.
- 25 16. A method of treating a condition selected from the group consisting of anxiety, depression, substance abuse, neuropathic pain, acute pain, migraine, asthma, cough and improved cognition, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the composition of Claim 9.
- 30 17. The use of a compound as in Claim 1 for the preparation of a medicament for the treatment of (a) anxiety, (b) depression, (c) substance abuse, (d) neuropathic pain, (e) acute pain, (f) migraine, (g) asthma, (h) cough or for (i) improved cognition, in a subject in need thereof.

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